Health effects of passive smoking · 8

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Passive smoking and risk of adult asthma and COPD: an update

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The number of published studies on passive smoking as a risk factor for adult onset asthma and chronic obstructive pulmonary disease (COPD) is small compared with the number on the adverse health effects of passive smoking on childhood respiratory symptoms and diseases. The paucity of research among adults may partly be due to a number of factors that make it difficult to design studies of these non-malignant respiratory diseases. The potential for misclassification of smoking status, with former or current smokers categorised as passive smokers, has been a longstanding concern in studies that rely on self reports of past smoking habits. Measuring past passive smoke exposure presents a major challenge in studies of chronic diseases that may become clinically apparent only after 20 or more years of exposure. Over-reporting of symptoms that subjects attribute to passive smoking is increasingly likely as public awareness of passive smoking increases. Also, it is difficult to measure lifetime exposure to the number of other confounding agents that are risk factors, which must be controlled for in studies of passive smoking.

While causation of asthma and COPD from passive smoking may not be directly demonstrable, it is possible to infer causal relationships from the concordance of scientific evidence, and Hill's nine criteria for causal association provide a useful guide for evaluating available evidence.[1] The nine criteria include strength of association, consistency, specificity, temporality, dose-response, plausibility, coherence, experimental evidence, and analogy. Of these criteria, plausibility, coherence, and analogy are fulfilled in relation to COPD by the established association of active cigarette smoking with chronic airflow obstruction. However, the criteria of specificity and experimental evidence have little relevance for human diseases associated with cigarette smoking.[2] Of the remaining criteria, strength of association, consistency, temporality, and dose-response have the greatest relevance for evaluating the evidence on passive smoking and adult onset asthma and COPD.

Despite the complexities of studying passive smoking and adult asthma and COPD, the literature on these topics has been growing since the mid 1980s. Summaries of the literature are contained in comprehensive reviews on the health effects of passive smoking that have been published in the USA[3–5] and Europe.[6] The objectives of this review are to summarise briefly the findings from these earlier reports, to update the literature based on more recent publications, and to evaluate the available evidence in the context of criteria for making causal inferences.

Previous reviews of passive smoking

In the 1986 report of the US Surgeon General[3] on "The Health Consequences of Involuntary Smoking" the available literature on passive smoking and non-malignant respiratory diseases in adults was limited to two references on chronic respiratory symptoms[7 8] and five on pulmonary function.[9–13] The report concluded that chronic respiratory symptoms of cough, phlegm, or wheeze among non-smokers were not associated with smoking by their spouses. For pulmonary function the main conclusion was that "healthy adults exposed to environmental tobacco smoke (ETS) may have small changes on pulmonary function testing, but are unlikely to experience clinically significant deficits in pulmonary function as a result of exposure to ETS alone". However, for children of parents who smoke the report concluded that the children "have small differences in tests of pulmonary function when compared with the children of non-smokers. Although this decrement is insufficient to cause symptoms, the possibility that it may increase susceptibility to COPD with other agents in adult life, e.g. active smoking or occupational exposures, needs investigation."

The National Research Council[4] also published a comprehensive review on ETS in 1986. However, because of the limited literature on passive smoking and non-malignant respiratory diseases among adults, little discussion on asthma or COPD was provided. The report did conclude that "it is unlikely that exposure to ETS can cause much emphysema" and "as one of the many pulmonary insults, however, ETS may add to the total burden of environmental factors that become sufficient to cause chronic airway or parenchymal disease."

In the comprehensive review published in 1992 by the US Environmental Protection Agency[5] entitled "Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders" there was one study of the risk of

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passive smoking and COPD[14] but no literature on passive smoking and risk for asthma among adults. This report included a review of six studies[14–19] on passive smoking and adult respiratory symptoms and lung function published since the 1986 report of the US Surgeon General. Based on these more recent studies the US Environmental Protection Agency concluded that ETS exposure "may increase the frequency of respiratory symptoms in adults" and that these "effects are estimated to be 30–60% higher in ETS-exposed non-smokers compared to unexposed nonsmokers." Similarly, the report concluded that "adult nonsmokers exposed to ETS may have small reductions in lung function (approximately 2.5% lower mean FEV_1)."

Thus, in the three major reviews of the health effects of passive smoking published in 1986 and 1992, respiratory symptoms and effects on lung function were the major non-malignant respiratory disease outcomes among adults for which reports were available. However, no available literature directly examined the association between passive smoking and asthma, and only one publication was available for COPD. By 1992 the evidence suggested that passive smoking was associated with respiratory symptoms and small decrements in lung function among adults. Evidence since 1992 will now be reviewed.

Asthma

Since the 1992 publication of the US Environmental Protection Agency a limited number of studies have been published on passive smoking and asthma among adults, and these studies can be characterised as aetiological and morbidity. The aim of the aetiological studies has been to determine the association between passive smoking and the diagnosis of asthma among adults. While the onset of asthma during infancy and childhood may be associated with ETS exposure[3 20] and persist into adulthood, this literature was the subject of another recent review.[20] In contrast to aetiological studies, morbidity studies have examined the role of passive smoking in causing symptoms or worsening lung function in patients with asthma.

AETIOLOGICAL STUDIES

In 1993 Hu *et al*[21] surveyed 1469 young adults aged 20–22 years from Los Angeles and San Diego. Their passive smoke exposure was determined from parental reports that had been obtained in 1986 as part of a school-based smoking prevention programme. Maternal and paternal smoking were associated with ever having physician-diagnosed asthma (OR = 1.6 (95% CI 1.1 to 2.3) and 1.3 (95% CI 0.9 to 1.8)), respectively. Similar results were found for current asthma with maternal smoking (OR = 1.6 (95% CI 1.0 to 2.4)) and paternal smoking (OR = 1.4 (95% CI 1.0 to 2.1)). Hu and coworkers also found a dose-response relationship with the amount smoked and the number of parents smoking. The highest risk of having physician-diagnosed asthma (OR = 2.9 (95% CI 1.6 to 5.6)) and current asthma (OR = 3.3 (95% CI 1.7 to 6.4)) was associated with both parents smoking compared with neither parent smoking.

Greer *et al*[22] examined the association between workplace exposure to ETS and new onset asthma among 3577 Seventh Day Adventists from Southern California followed between 1977 and 1987. At enrolment the mean age of the subjects was 56.5 years. During the 10 year follow up period 78 subjects developed asthma, and workplace exposure to ETS was a significant risk factor (RR = 1.5 (95% CI 1.2 to 1.8)) after controlling for sex, education, childhood history of obstructive airway disease before 16 years of age, and ambient ozone levels. In a survey of 4197 Swiss residents aged 18–60 years Leuenberger *et al*[23] found that exposure to ETS at home and work during the past 12 months was significantly associated with doctor-diagnosed asthma (OR = 1.4 (95% CI 1.0 to 1.9)).

Because active cigarette smoking has been associated with an increased risk of developing occupational asthma due to IgE inducing agents,[24] it is plausible to hypothesise that passive smoking may also contribute to the development of occupational asthma in non-smokers. While workplace exposure to ETS has been associated with asthma among adults,[22 23] no published investigations have been made of the interaction of ETS exposure at work and exposure to specific occupational agents.

MORBIDITY STUDIES

In a 1994 review Tredaniel *et al*[5] summarised results of the effect of ETS exposure on respiratory symptoms and lung function from four observational studies of patients with respiratory allergies and five experimental studies of patients with asthma. The authors concluded that "conflicting evidence exists on the association in asthmatic patients between ETS exposure and appearance of symptoms and functional abnormalities (including change in bronchial responsiveness)". Three studies, two clinical[25 26] and one experimental,[27] that were not included in the review by Tredaniel *et al*[5] provide evidence of an adverse effect of ETS exposure on adult patients with asthma.

To determine the clinical impact of ETS exposure on patients with asthma, Jindal *et al*[25] enrolled 200 never-smoking patients with asthma aged 15–50 years from a chest outpatient clinic in India and categorised the patients into ETS exposed and not exposed. Patients who were exposed had a higher rate of acute episodes of asthma, emergency department visits, absences from work, parenteral bronchodilator use, and steroid use. In addition, patients who were exposed had greater impairment of lung function (forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) = 68.7) than those who were not exposed (FEV_1/FVC = 78.4).

Ostro *et al*[26] enrolled 164 asthmatics with a mean age of 45.5 years from a clinic in Denver, Colorado. For as long as three months these patients recorded daily information about

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symptoms, medication use, physician and emergency room visits, and indoor exposures. After correcting for repeated measures and autocorrelation, exposure to ETS was associated with moderate or worse shortness of breath (OR 1.34 (95% CI 0.84 to 2.15)), moderate or worse cough (OR 1.15 (95% CI 0.97 to 1.36)), and restriction in activity (OR 1.61 (95% CI 1.06 to 2.46)).

To determine the acute effects of ETS exposure on lung function Danuser *et al*[27] conducted an experimental study that included 20 non-smoking subjects, 10 with airways hyperreactivity to methacholine and 10 normoreactive subjects. Subjects inhaled increasing concentrations (2, 4, 8, 16, 32 ppm CO) of sidestream tobacco smoke through a mouthpiece during two minutes of tidal breathing and spirometric values were measured 30 seconds and 90 seconds after inhalation. None of the normoreactive subjects had a change in lung function with ETS inhalation. The hyperreactive subjects had significant decreases in FEV_1, FVC, and MEF_{50}, with the greatest decline after the lowest dose of 2 ppm CO. At this exposure the mean fall in FEV_1 was 6.3% and five of the 10 subjects had a decrease in FEV_1 of more than 10%.

SUMMARY

Although the available literature is limited, it does show that exposure to ETS is associated with an increased risk of adult onset asthma and with worsening of respiratory symptoms and lung function in adult asthmatics. Adults exposed to ETS at home or in the workplace have a 40–60% increase in risk for asthma compared with adults who are not exposed in these places. In one study a dose-response relationship was found between the number of parents smoking in the home and the risk of asthma among young adults. Finally, ETS exposure worsens respiratory symptoms and lung function among adult asthmatics.

COPD

COPD is a non-specific term that is defined differently by clinicians, pathologists, and epidemiologists, with each using different criteria based on symptoms, physiological impairment, and pathological abnormalities.[28] The hallmark of COPD is the slowing of expiratory airflow measured by spirometric testing, with a persistently low FEV_1 and low ratio of FEV_1 to FVC despite treatment. Although chronic bronchitis and emphysema are classically associated with the term COPD, they do not invariably involve chronic airways obstruction and recent evidence suggests that changes in the structure and function of the bronchioles are fundamental for the development of smoking induced COPD.[29 30] Active cigarette smoking is the single-most important risk factor for COPD, with 85–90% of COPD related mortality attributable to active cigarette smoking.[31 32] However, these results also suggest that 10–15% of COPD cases are attributable to other risk factors such as ETS, occupational exposures, and genetic factors.

Using survey data from three US National Health and Nutrition Examination Surveys (NHANES), Whittemore *et al*[33] determined the prevalence of COPD (self-reports of doctor-diagnosed chronic bronchitis or emphysema) among 12 980 lifelong non-smokers aged 18–74 years. Overall, 3.7% of men and 5.1% of women reported physician-diagnosed COPD, and the prevalence increased with age and among the economically disadvantaged. While this study was limited to self-reports of COPD and lacked information on ETS exposure, these results provide evidence that COPD is not uncommon among non-smokers and that risk factors other than active cigarette smoking, such as ETS, may contribute to the development of COPD in non-smoking aduits.

The measures of COPD used in the literature vary because COPD is a non-specific term that may be measured in a number of different ways. For this discussion the relevant literature is organised into three categories of investigation based on these different measures of COPD. Two categories of investigation relied on indirect measures of COPD, including self-reports of respiratory symptoms or diagnosis of COPD, or effects on lung function level. The third category of investigation used direct measures of COPD—mortality and hospitalisation. The subsequent discussion summarises results from each of these types of investigation. In contrast to asthma, the available literature has focused on ETS exposure as a risk factor for COPD and not as an exposure that may contribute to worsening symptoms or lung function in patients with COPD.

SELF-REPORTED OUTCOMES

Since 1992 several investigations have been published[23 34 35] (table 1) that provide further support for the conclusion of the US Environment Protection Agency[5] that ETS exposure "may increase the frequency of respiratory symptoms in adults" and that these "effects are estimated to be 30–60% higher in ETS-exposed non-smokers compared to unexposed nonsmokers". These newer investigations have relied on self-reported information about respiratory symptoms and doctor diagnoses and they have combined asthma, chronic bronchitis, and emphysema to define chronic obstructive airways diseases. Although these studies have been conducted in three separate locations and used different definitions of passive smoke exposure, including different periods and locations of exposure, the results are remarkably similar and further strengthen the evidence that passive smoking is associated with chronic respiratory symptoms and reports of COPD.[36]

While the relevance of self-reported respiratory symptoms and doctor diagnoses to COPD may be questioned, Jaakkola *et al*[37] provide evidence that these reports may be associated with an accelerated rate of lung function decline that, over many years, may result in the development of COPD. During an eight year period they determined the rate of change of FEV_1 among 391 subjects aged 15–40 years and

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Table 1 Selected investigations of associations between passive smoking, chronic respiratory symptoms, and self-reports of doctor-diagnosed asthma, chronic bronchitis and emphysema

Reference no.	Study population	Study period	Exposure assessment: Periods	Exposure assessment: Location	Other exposures	Outcome	Results
34	Adventist Health Study, (n = 3914), ≥25 years of age	1977–87	Childhood and adulthood	Home and work	Outdoor TSP, past smoking	Symptoms and doctor-diagnosed asthma, chronic bronchitis, emphysema	Childhood exposure only RR = 1.1 (95% CI 0.7 to 1.7) Childhood and past adult exposure RR = 1.7 (95% CI 1.3 to 2.2) Childhood and current adult exposure RR 2.0 (95% CI 1.2 to 3.2)
35	Philadelphia, 219 non-smokers with self-report of obstructive respiratory disease, 657 controls	1985–86	Adulthood	Home	—	Doctor-diagnosed asthma, chronic bronchitis, or emphysema	Passive smoking: <1 ppd, OR = 1.2 (95% CI 0.8 to 1.7) ≥1 ppd, OR = 1.9 (95% CI 1.2 to 2.9)
23	Eight areas in Switzerland, (n = 4197), 18–60 years of age	—	Past 12 months	Home and work	—	Self-reports of symptoms and diagnosis	Passive smoking: Wheezing, OR = 1.9 (95% CI 1.4 to 2.7) Chronic bronchitis, OR = 1.7 (95% CI 1.3 to 2.2) Dyspnoea, OR = 1.5 (95% CI 1.2 to 1.8) Doctor-diagnosed asthma, OR = 1.4 (95% CI 1.0 to 1.9)

TSP = total suspended particulates.

found that subjects who developed wheezing, dyspnoea, and doctor-diagnosed asthma had greater rates of decline in lung function (−12.3 ml/year, −16.2 ml/year, and −42.6 ml/year, respectively) compared with subjects without symptoms of asthma.

LUNG FUNCTION

Another approach investigators have taken to determine the potential risk of passive smoking for the development of COPD is to examine the relationship between lung function level and passive smoking.[6 38] Although longitudinal data on the effects of active or passive smoking and development of COPD are not available from childhood through adulthood, current evidence suggests that the development of COPD in adults may result from impaired lung development and growth, premature onset of decline in lung function, and/or accelerated decline in lung function.[38–40] In utero airway development and alveolar proliferation to 12 years of age are critical to the mechanical functioning of the lungs, and impaired lung growth in utero from exposure to maternal smoking may begin a process that leads to development of COPD. Exposure to ETS in infancy and childhood and active smoking during childhood and adolescence contributes to impaired lung growth, which limits the maximum level of lung function attained[38] and may increase the risk for developing COPD. The impact of passive smoking during adulthood on lung function and risk for development of COPD remains controversial.[6] However, because it is established that active cigarette smoking in adulthood leads to accelerated decline in FEV_1 among susceptible smokers and ultimately to the development of clinically apparent COPD, passive smoking must also be considered a biologically plausible risk factor.

In 1994 Tredaniel *et al*[6] reviewed the available evidence on exposure to ETS and adult non-neoplastic respiratory diseases that included 18 publications on lung function and ETS exposure published between 1977 and 1992. Of these 18 publications eight found no effect of ETS exposure on lung function and 10 demonstrated small decrements in lung function with ETS exposure. The authors noted a number of limitations of the available studies including lack of information on potential confounders and childhood exposures to ETS. Further, when detected, the magnitude of decrement associated with ETS exposure was small, raising questions about the clinical relevance for development of COPD.

Since the review published by Tredaniel *et al*,[6] results of three subsequent investigations of passive smoking and lung function have been published[41–43] (table 2) and, as in the previous review, the results were inconsistent. Jaakkola *et al*[41] examined the rate of decline of FEV_1 and FEF_{25-75} over an eight year period in a group of 117 non-smokers aged 15–40 years and found no relation between ETS exposure and change in lung function. However, the age of subjects spanning the period of lung growth, plateau, and decline may have limited their ability to detect an adverse effect of ETS. Among 1033 adults aged 40–69 years living in Beijing, China, Xu *et al*[42] found significantly lower levels of FEV_1 and FVC, after controlling for potential confounders, among subjects exposed to ETS at home or work compared with subjects not exposed. Frette *et al*[43] did not find an association between ever living with a smoker and level of FEV_1, FVC, or FEF_{25-75} among an elderly population aged 51–95 years living in Southern California. However, a difference may not have been detected because subjects passively exposed were significantly younger than subjects not exposed.

Non-specific bronchial hyperresponsiveness has been associated with an accelerated decline in lung function and may identify active smokers susceptible to the development of COPD.[44 45] While this evidence provides a plausible link between passive smoking, bronchial hyperresponsiveness, and COPD, limited information is available on these relationships. Menon *et al*[46] exposed 31 smoke-sensitive subjects with asthma and 39 smoke-sensitive subjects without asthma to ETS for four hours in a test chamber. Of the subjects without asthma, 18% had increased bronchial reactivity at six

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Table 2 Selected investigations of passive smoking and lung function level among adults

Reference no.	Study population	Study period	Exposure assessment: Periods	Exposure assessment: Location	Other exposures	Outcome	Results
41	117 never smokers, 15–40 years, Montreal	1980–89	Lifetime and past three days	Home and work	—	Rate of FEV_1 and FEF_{25-75} change over 8 years	No relation between ETS exposure and change in lung function
42	1033, 10–69 years, Beijing	1986	Current	Home and work	Occupation, indoor coal stoves	FEV_1 and FVC level	*Exposure* / *FEV₁ (ml)* / *FVC (ml)*: Work or home −121* −182*; Work and home −145* −189*
43	415 never smokers, 51–95 years, Southern California	1988–91	Lifetime	Home	—	FEV_1, FVC, FEF_{25-75} level	*Non-smokers exposed* / *Non-smokers not exposed*: FEV (l) Men 3.00 3.14; Women 2.12 2.12; FVC (l) Men 3.90 4.10; Women 2.72 2.71; FEF_{25-75} (l/s) Men 2.66 2.80; Women 2.00 1.99

*Estimated decrement in lung function among non-smokers exposed compared to non-smokers not exposed, $p<0.05$.

hours after exposure, 10% at 24 hours, and 8% at three weeks. These results suggest that bronchial hyperreactivity may result from ETS exposure even in asymptomatic non-asthmatic subjects.

COPD MORTALITY AND HOSPITALISATION

The association between COPD and passive smoking has been directly examined in four investigations including two mortality studies[49 50] and two case-control studies of hospital admissions for COPD.[14 51] In a population based cohort of 91 540 non-smoking Japanese housewives aged 40 years and older, Hirayama[49] determined cause of death during the period 1966 to 1979 and found 66 deaths from emphysema and asthma. Compared with women whose husbands were non-smokers, women whose husbands were ex-smokers or smoked 19 cigarettes or less had a 29% increased risk of death from emphysema or asthma, and if their husband smoked 20 or more cigarettes per day a 49% increased risk of death from emphysema or asthma. Because of small numbers these results were not statistically significant. During the period 1963–75 Sandler *et al*[50] determined causes of death among white residents of Washington County, Maryland, USA and examined associations with passive smoke exposure among 10 799 residents who reported that they were never smokers in 1963 and had household smoking exposure. Risk of death from emphysema and bronchitis was increased in women (RR 5.7 (95% CI 1.2 to 26.8), n = 13) but not in men (RR 0.9 (95% CI 0.2 to 5.3), n = 6).

Lee *et al*[51] and Kalandidi *et al*[14] used the case-control design to examine the association between passive smoking and COPD. As part of a hospital based case-control study in 10 hospital regions of England conducted from 1977 to 1982, Lee *et al*[51] found a small increase (OR = 1.3) in risk for chronic bronchitis with the highest category of passive smoke exposure, but this estimate was based on only two cases. Kalandidi *et al*[14] studied 103 ever married women aged 40–79 years who, on two separate occasions, denied ever smoking and who were admitted to an Athens hospital with a diagnosis of chronic obstructive lung disease. The control group comprised 179 ever married non-smoking women who were visiting the hospital. Compared with women whose husbands never smoked, women whose husbands smoked had an increased risk of COPD with an OR of 2.6 (90% CI 1.3 to 5.0) for husbands who smoked a pack per day or less and an OR of 1.5 (90% CI 0.8 to 2.7) for husbands who smoked more than a pack per day.

SUMMARY

The occurrence of COPD and risk factors for COPD among non-smokers has received limited attention. Results from a nationwide population based survey in the USA suggests that 3–5% of non-smokers may be affected.[33] However, these results were based on self-reports and will require further confirmation of the diagnosis before the potential public health impact is determined. Passive smoking as a risk factor for COPD among non-smokers has been demonstrated in a number of studies that have used diverse methods for defining COPD, including self-reports of doctor diagnosis, physician diagnosis, and mortality data. However, studies that have used self-reported diagnosis are limited by the inclusion of doctor-diagnosed asthma in their definition of COPD. While various measures of COPD have been associated with passive smoking, the effects of passive smoking on lung function have been inconsistent and part of the inconsistency may be a result of a number of methodological differences between the studies. If passive smoking causes a decrement in lung function, the magnitude of effect is small, which raises concern about how this small effect could result in the diagnosis of COPD. Further, little is known about the effects of ETS exposure on respiratory symptoms or lung function among patients with COPD.

Conclusions

The complexity of investigations of passive smoking as a risk factor for adult onset asthma and COPD may have contributed to the limited number of publications on these topics

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that have appeared since the comprehensive reviews on the health effects of involuntary smoking published in 1986 by the US Surgeon General and the National Research Council. Because there was no available literature on asthma or COPD in 1986, the conclusions of these reports were limited to the effects of passive smoking on chronic respiratory symptoms and on pulmonary function. At that time there was no evidence that cough, phlegm, or wheeze was associated with passive smoking by spouses, and among healthy adults ETS was associated with small changes in pulmonary function. Subsequent investigations provide evidence of a small and consistent association between passive smoking and respiratory symptoms (table 1). However, making causal inferences from the available data is difficult because of the weak associations and because of the limited data on the temporal relationship[34] and dose-response[35] between ETS exposure and development of respiratory symptoms. Compared with respiratory symptoms the evidence for a causal association between ETS exposure and lung function is even weaker (table 2).

The main additions to the literature on passive smoking and non-malignant respiratory diseases have been from investigations that have directly examined associations between passive smoking and asthma and COPD. Based on self-reports of doctor diagnosis, adults exposed to ETS at home or in the workplace have a 40–60% increased risk for asthma (table 1). Further, ETS exposure worsens respiratory symptoms and lung function among adult asthmatics. Passive smoking as a risk factor for COPD among non-smokers has been demonstrated in a number of studies that have used diverse methods for defining COPD, including self-reports of doctor diagnosis, physician diagnosis, and mortality data. While growing evidence suggests that passive smoking is a risk factor for adult onset asthma and COPD, the magnitude of the associations is small. However, additional evidence on the relationship between passive smoking and asthma and COPD is needed to fulfil the criteria for causality, particularly the criteria of temporality and dose-response.

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